National Center for the Design of Biomimetic Nanoconductors

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2 Oxford University
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4 Wabash College
5 University of Southern California
7 Yale University
8 Sandia National Laboratories
9 Cornell University
10 Illinois Institute of Technology

For the Nanomedicine Applicants Meeting January 27, 2005

The most powerful scientific minds have always recognized the power of interdisciplinary thinking--From: Isaac Newton:

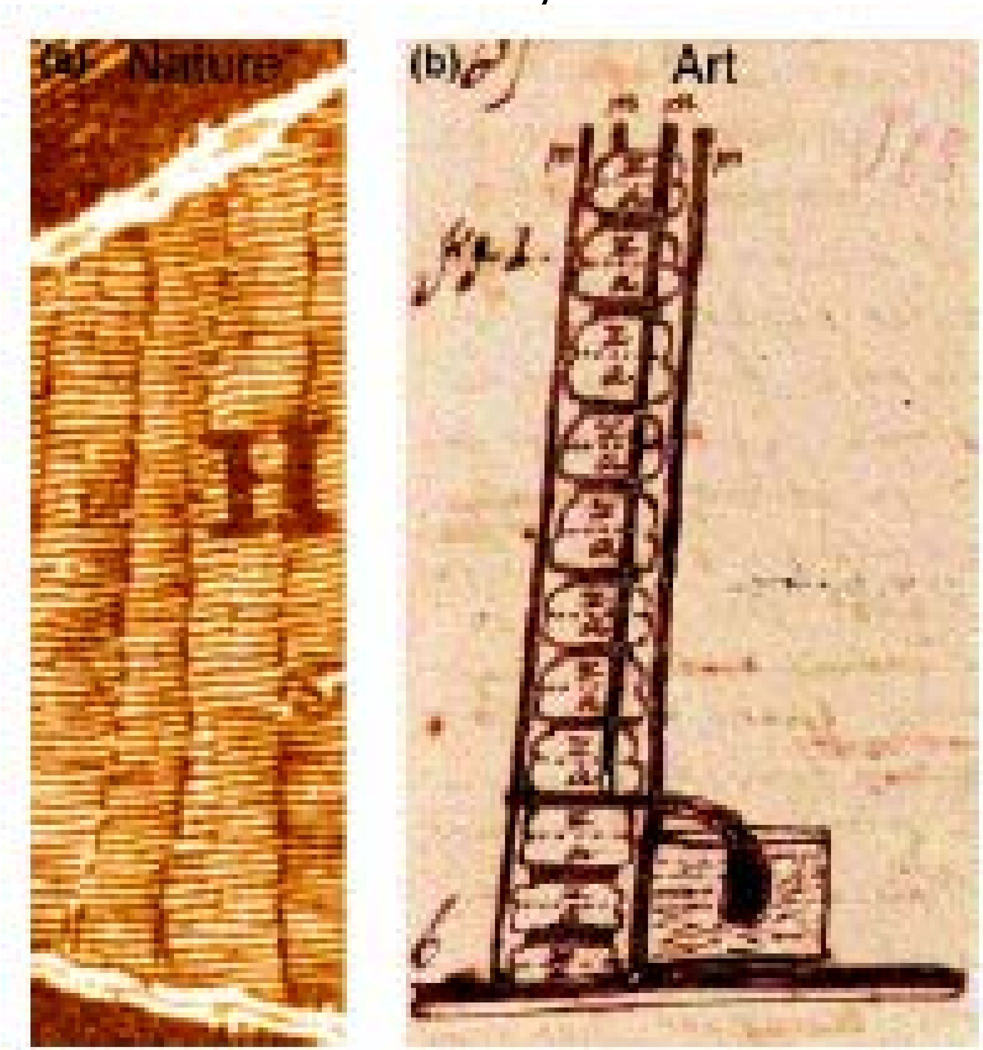
The Mathematical Principles of Natural Philosophy

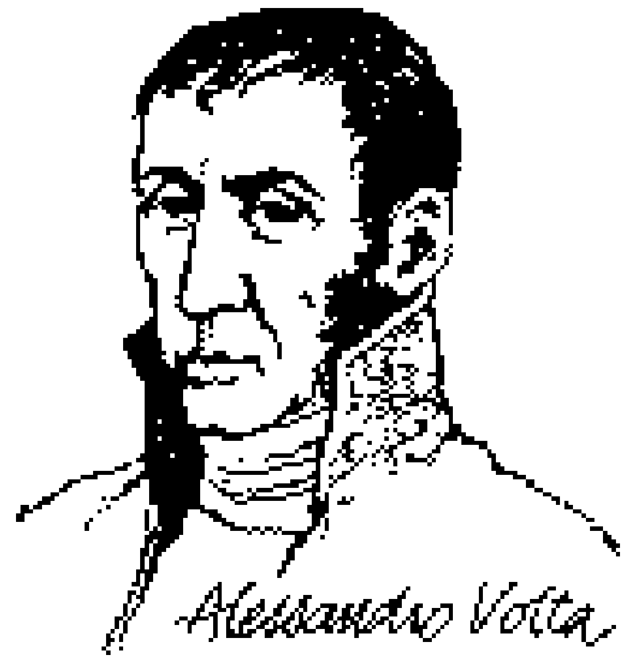
RULE II

Therefore to the same natural effects we must, as far as possible, assign the same causes.

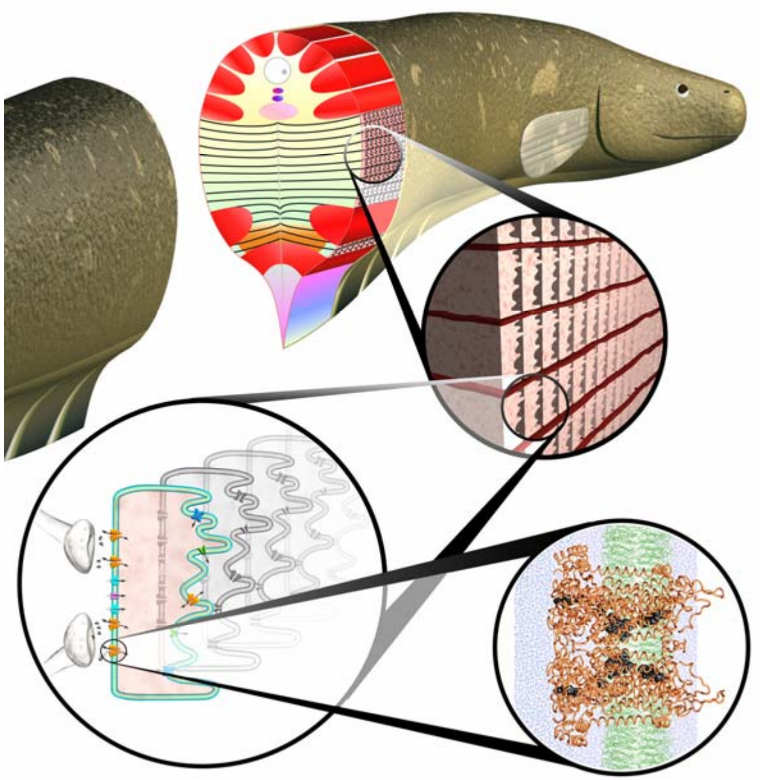
As to respiration in a man, and in a beast; the descent of stones in Europe and in America; the light of`our culinary fire and of the sun; the reflection of light in the earth, and in the planets

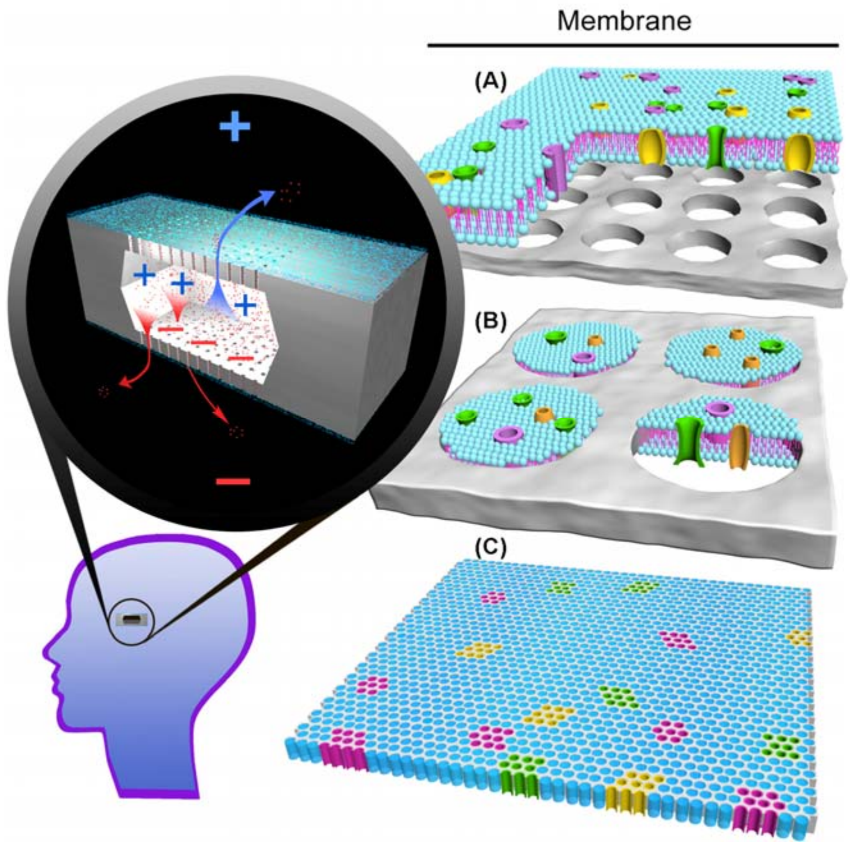
An interdisciplinary scientist of the 18th Century—Volta, inspired by the electric organ of the electric eel, invented the battery





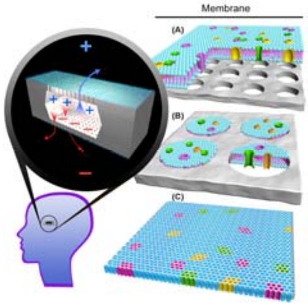
The Biobattery—Nanoengineering inspired by the Electric Eel





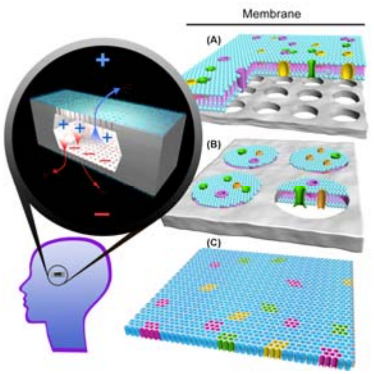
Initial Design Target---Implantable Power Source for the Artificial Retina.

- Developed by a team led by our co-Pi Mark Humayan at Southern California, the artificial retina pairs a retinal implant with a video camera mounted on a pair of sunglasses. It is designed for patients for which the retina has been damaged. The implant, when activated by the camera, stimulates the remnant photoreceptor cells capable of electrical activity which in turn stimulate the optic nerve.
- A device has been implanted in six blind human subjects, with restoration of pattern and movement sensing.
- It would be highly desirable to produce an implantable biocompatible battery to power the retinal implant.



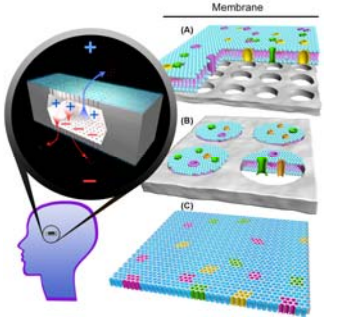
The Minimal Molecular Parts List

- An activator (Chemically, optically, or otherwise sensitive ion channel)
- Electrical Current Generators (Voltage-gated sodium channels and delayed rectifier potassium channels)
- Activity modulators (Other types of potassium channels; i.e., A-currents, etc.)
- Housekeeping transporters to maintain electrochemical and osmotic gradients (ATPases and coupled transporters)



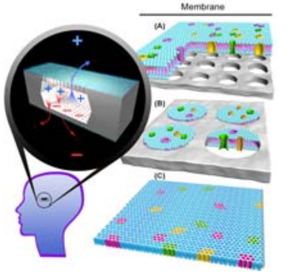
Overall construction

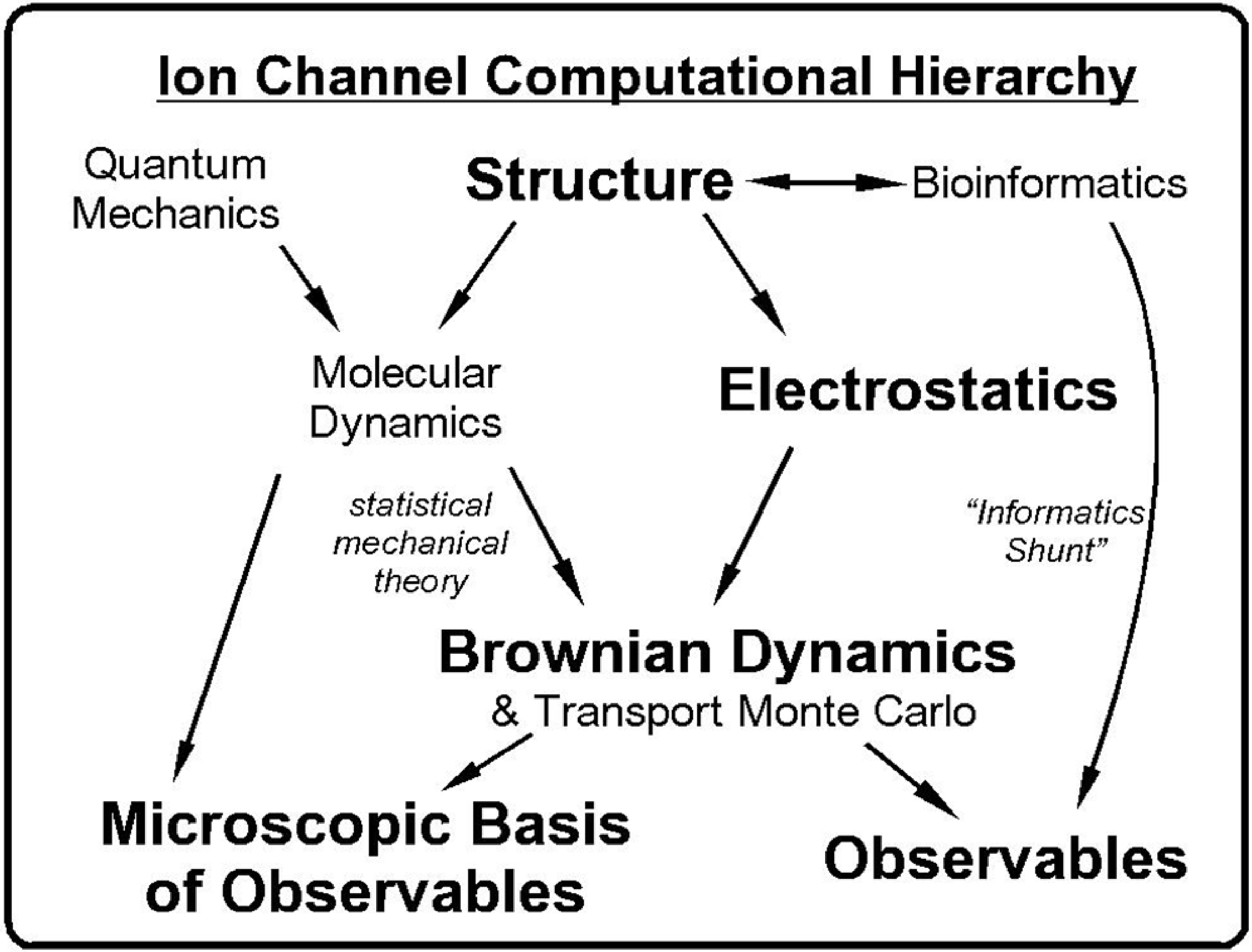
- Transporters at the surface of cells (“cells” in both the biomimetic and the battery meaning.)
- Surface framework comprising silicon nanopore arrays containing transporters.
- Cells in series increase voltage; cells in parallel increase current.



Scientific Challenges to be overcome

- Multiscale simulation of ion transporters, and dynamical simulation of whole cells, as a foundation of computer aided design.
- Molecular engineering based on proteins, synthetic transporters, and chemically modified nanopores.
- Prototype and device fabrication and testing.

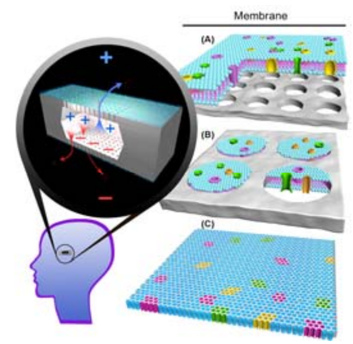



Ion Channel Computational Hierarchy
Quantum Mechanics
Structure
Bioinformatics
Molecular Dynamics
Electrostatics
statistical mechanical theory
"Informatics Shunt"
Brownian Dynamics
& Transport Monte Carlo
Microscopic Basis of Observables
Observables

T1. Proton permeation and transfer reactions using coupled stochastic/molecular dynamics methods

Kevin Leung and Susan Rempe,
Sandia National Laboratories

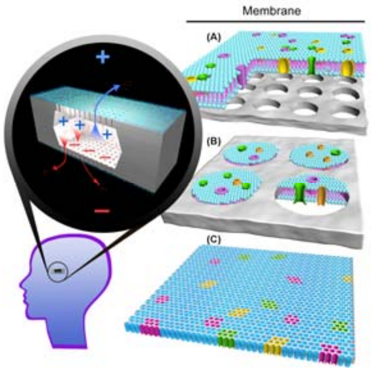
Product: Software that will permit the computation of proton hopping among titratable sites in electrolytes and in ion transporters.



T2. Multiscale Analysis of Water and Ion Transport in Synthetic Nanopores (Theoretical complement to Brinker lab work on chemically modified nanopores).

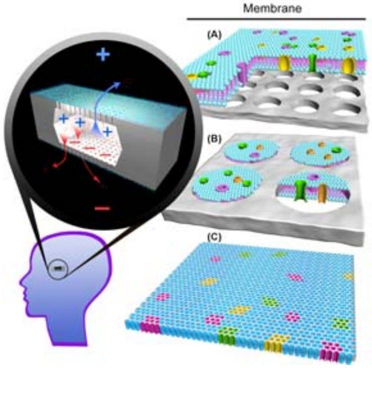
1. Quantum mechanical analysis of the synthetic pores
2. Molecular dynamics of transport in the pores
3. Continuum Analysis

Narayana Aluru and Umberto Ravaioli, University of Illinois.



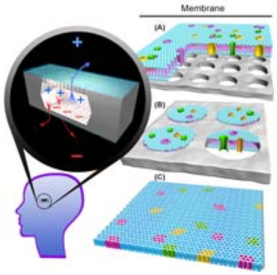
T3. Advances in Electrostatics (For support of several computational methods)

Umberto Ravaioli, University of Illinois, and Marco Saraniti, Illinois Institute of Technology



T4. Development of Polarizable Force Fields for Nanoconductor Simulation

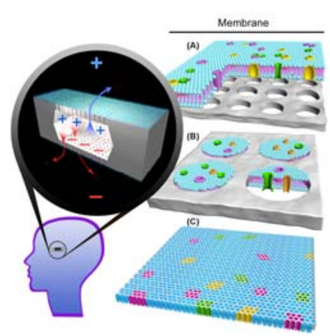
T5. Grand Canonical Monte Carlo/Brownian Dynamics for Simulation of Ion fluxes in Porins and Alpha-Hemolysin Variants (Simulating the results of the Bayley experiments.)



Benoit Roux, University of Chicago

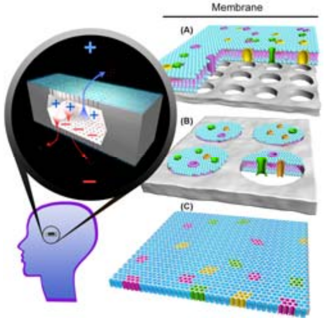
T6. Molecular Dynamics simulations of lipid bilayer membranes assembled on ordered nanoporous Silica thin films:

Scott Feller, Wabash College and Larry Scott, Illinois Institute of Technology



T7. Developing an Integrated Modeling Platform for the Mixed or Compartmentalized Interiors of Cells, Organelles and Devices.

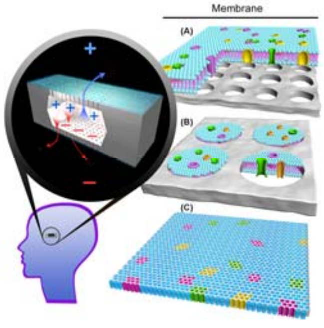
Steve Plimpton, Sandia National Laboratories; and Xinguang Zhu, University of Illinois



T8. Integrating the Computational Approaches into a Seamless, User-Friendly, Grid-Enabled Cell and Nanodevice Computer-Aided Design Environment

Eric Jakobsson, University of Illinois, and Mike McLennan, Purdue

D. Overall Design of the Biobattery



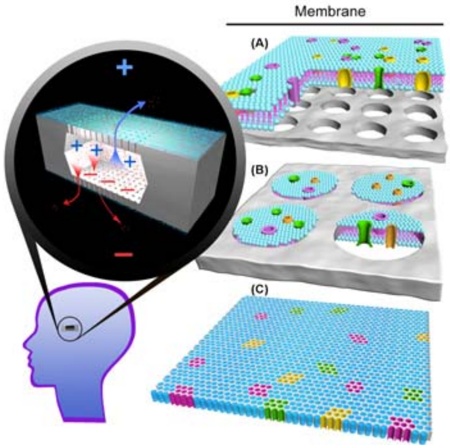
David LaVan, Yale and Mark Humayun, University of Southern California

E1. **Materials and processes to stabilize transporters in synthetic membranes.**

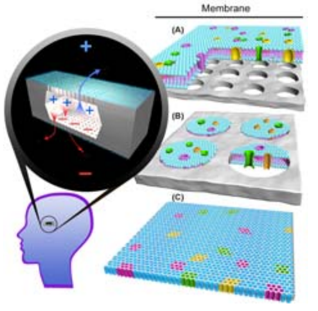
Jeff Brinker, University of New Mexico and Atul Parikh, University of California-Davis

E2. Development of fully synthetic channels

Jeff Brinker, University of New Mexico.



E3. Preparation of supported architectures containing multiple transporters.

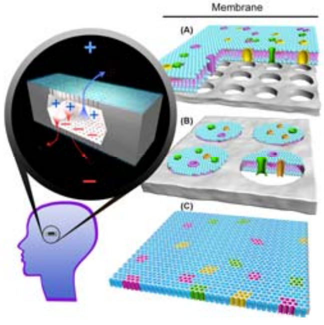


Jeff Brinker, New Mexico, and
David LaVan, Yale

E4. Engineering nanotransporters with specific functionality - αHL as a model system.

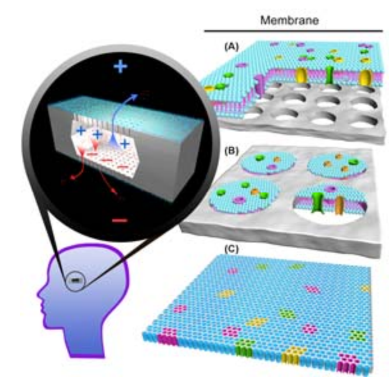
Light-switchable Ca2+ release through the αHL pore

Hagan Bayley, Oxford



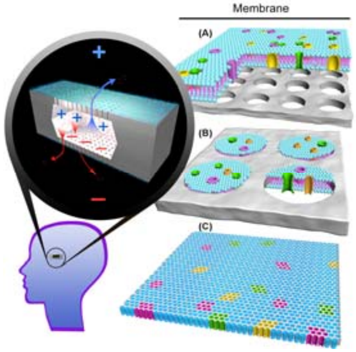
E5. Characterization of natural and synthetic transporters and membranes

Hagan Bayley, Oxford, Jeff Brinker, New Mexico, and David LaVan, Yale.



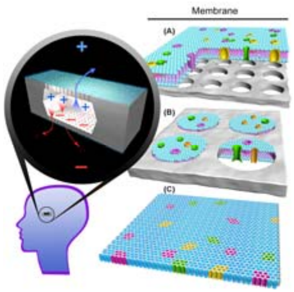
E6. New methods to pattern transporters onto membranes and control the lipidic microenvironment.

Jeff Brinker, New Mexico, and Atul Parikh, University of California-Davis

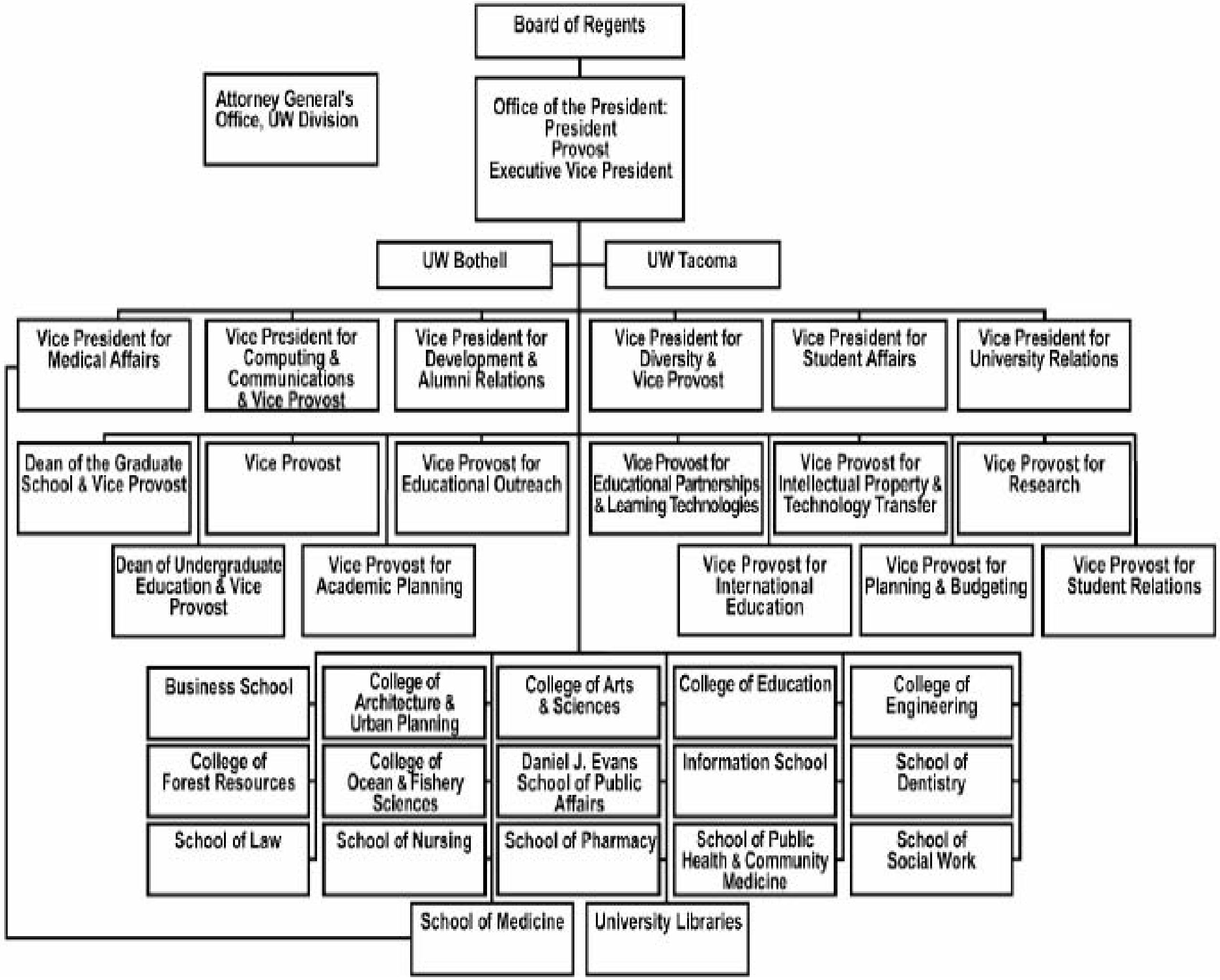


Bridging the Experimental-Computational-Design Divides

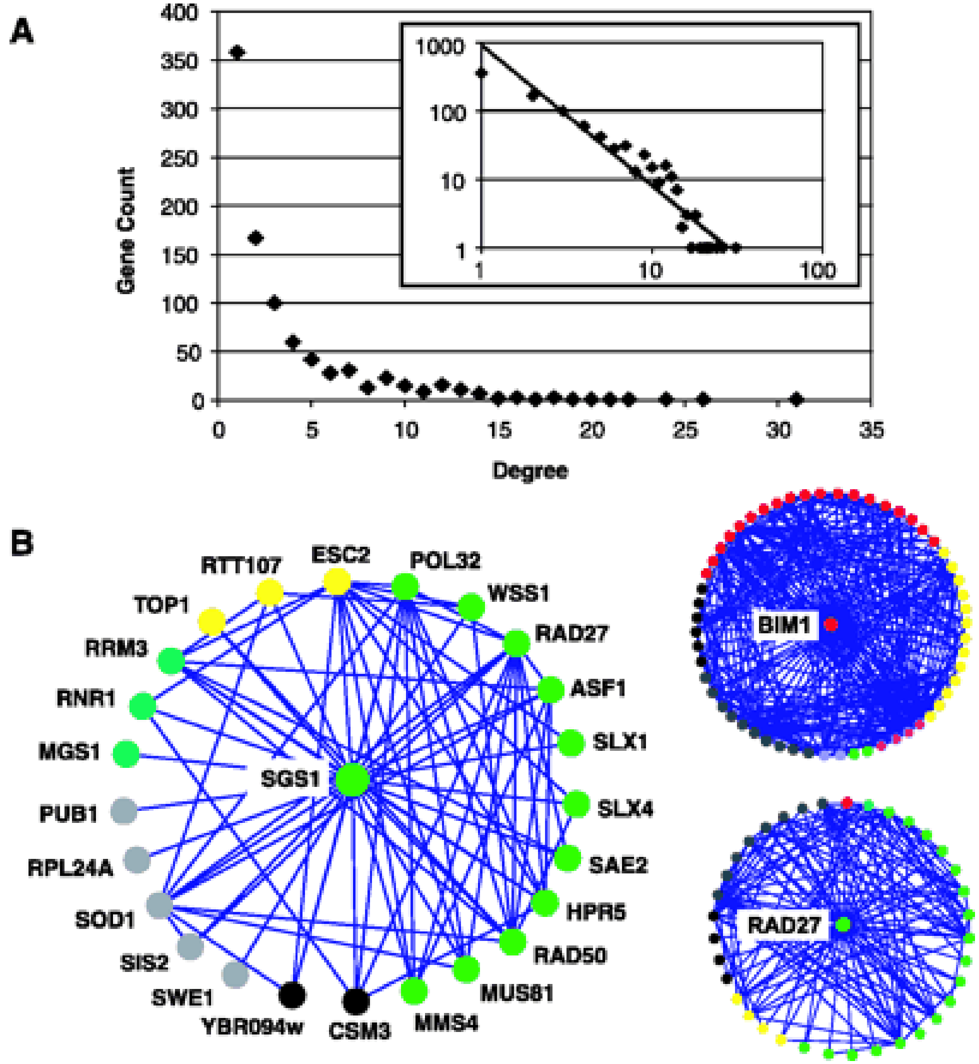
- Theory and computation in the Center will be validated by experiment in the Center.
- Experiment in the Center will be guided by theory and computation in the Center.
- Computation and theory in the Center will be focused on support of device design.



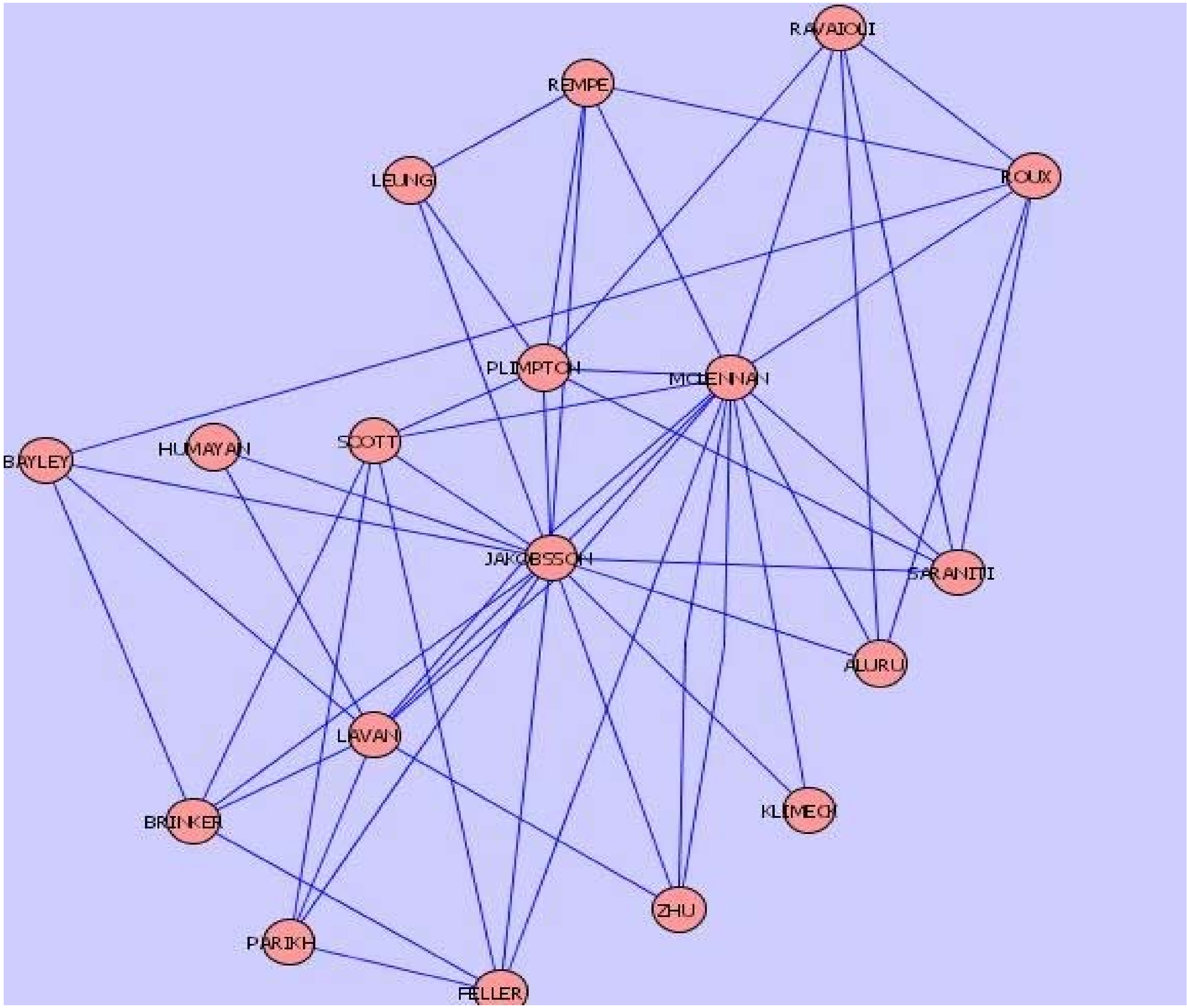
Official Organization Chart of the University of Washington—a typical official research university organization--guaranteed to fail if functional relationships followed the chart. The system only works at all because people create other connections not reflected in the official chart, but the system works poorly because the institution does not reward the creation of the other connections.



Organization charts that actually work (from Tong et al, Global mapping of the yeast genetic interaction network, *Science, 2-6-04*…). Typically, there are multiple paths between each pair of nodes.



An organization chart that we hope will work---the interaction network of participating investigators at The National Center for the Design of Biomimetic Nanoconductors. The Principal Investigator (Jakobsson) is at the center rather than the top. There are multiple alternative pathways to getting things done.



M. Sustained geographically distributed management will be by Macromedia Breeze, enhanced by our team.

Swaroop Shivarajapura, Purdue University

Principles of Organization

- “It’s surprising what you can accomplish when no one is concerned about who gets the credit.”---sign kept on the desk of Ronald Reagan
- Corollary: There is no limit to the pain and disruption potentially associated with priority and intellectual property disputes.

Broad agenda for 1st all hands meeting on February 3-4

- Establish operating procedures for the Center.
- Presentations of relevant science from the partners and planning for collaborative sub projects.
- Strategizing for seeking augmenting funds.